REMARKS/ARGUMENTS

Claims 9-12 are pending. Claims 9, 11 and 12 have been amended herein. Claims 1-8 and 13 have been cancelled without intending to abandon or to dedicate to the public any patentable subject matter.

Objection to the Claims

The Examiner has objected to the recitation of "GeneBank" in Claim 9. Applicants have deleted this misspelling from Claim 9.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected Claims 9-12 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. The Examiner does not delineate this rejection other than to reference "pages 3-4 of the office action mailed on 10/26/2007." Therein, the Examiner rejects Claim 6, and claims depending therefrom, as indefinite for recitation of the phrase "a wild-type GT gene" and "a normal GT protein." Applicants have previously cancelled Claim 6. Additionally, Claim 9 has been amended to delete the recitation of "a normal GT protein." As such, this rejection has been overcome by the amendments to Claim 9.

At pages 3-4 of the office action mailed on 10/26/2007, the Examiner also made claim rejections based on phrases recited in Claims 6 and 8. As Applicants have previously cancelled these claims, these rejections are moot.

The Examiner has also rejected Claim 9 due to the recitation of a GenBank Accession number, a PCR method and a pig GT cDNA sequence as indefinite as they appeared in Claim 9. Applicants have deleted these phrases from pending Claim 9.

The Examiner has rejected Claim 9 due to the recitation of the phrase "corresponding to." Applicants have amended Claim 9 to delete this phrase and substitute the transitional phrase "consisting of."

The Examiner has also rejected Claim 12 as reciting the phrase "SNU-P2 [Porcine NT Embryo]" in reference to Claim 9. Claim 12 has been amended to recite the steps of the claimed method without reference to Claim 9. Applicants therefore submit that Claim 12, as amended,

does not require antecedent support for SNU-P2 [Porcine NT Embryo].

Applicants therefore submit that the pending claims, as amended, are sufficiently definite to meet the requirements of 35 U.S.C. § 112, second paragraph.

Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected Claims 9-12 under 35 U.S.C. § 112, first paragraph, as lacking enablement for any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the claimed invention.

Specifically, the Examiner argues that the specification lacks enablement for the use of any porcine somatic cells other than fetal fibroblast cells. Applicants have amended Claim 9 to limit the claimed methods to the use of fetal fibroblast cells.

Additionally, the Examiner argues that the specification lacks enablement for the use of any PCR method to generate fragments of exon 9 of the GT pig gene. Applicants have amended Claim 9 to remove the recitation of the PCR method.

Additionally, the Examiner argues that the specification lacks enablement for the use of any non-viable SNU-P2[Porcine NT Embryo]. Applicants submit herewith a declaration by the Applicant of deposit of SNU-P2[Porcine NT Embryo] with the Korean Collection for Type Cultures (KCTC) which is an International Depositary Authority (IDA) recognized under the Budapest Treaty in compliance with 37 CFR § 2405. In light of this deposit and Applicants' declaration thereto, Applicants submit that the recitation of SNU-P2[Porcine NT Embryo] is enabled.

In view of the foregoing remarks regarding amendments to the claims and the deposit of claimed biological materials in compliance with the Budapest Treaty, Applicants submit that there is adequate enablement in the specification for Claims 9-12, as amended, and request the Examiner's rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claim Rejections Under 35 U.S.C. § 103

The Examiner has rejected Claims 9 and 12 under 35 U.S.C. § 103(a) as being obvious over **Day** (U.S. Patent Publication No. 2005/0120400) in view of **Mason** (U.S. Patent No. 5,576,201). The Examiner argues that Day teaches the method steps of the pending claims with

the exception of the use of a vector including a puromycin-resistant gene linked to an SV40 poly (A) sequence as required by the pending claims. For this limitation, the Examiner argues that Mason teaches a transducing vector containing a puromycin-resistant gene linked to a SV40 poly (A) sequence, and thus one of skill in the art would find it obvious to use the methods of Day and the puromycin-resistant gene linked to a SV40 poly (A) sequence removed from the rest of the vector, described by Mason, to arrive at the methods of the currently pending claims. The Examiner provides no motivation for one of skill in the art to combine the teachings of these two references but does state that one of skill in the art would be motivated because both "puromucin and G418 are commonly used selection marker used for select cells that have been transfected with target DNA vector, and SV 40 poly A sequences is commonly used in a vector for proper expression of cloned gene of interest." Applicants note that this is not actually a motivation to combine these references, but rather merely a statement that these two components which make up a vector are commonly known separately in the prior art.

The principle of producing a knockout pig is to remove a specific gene by constructing a targeting vector including both end portions ("flanking regions") of a specific gene which a user wants to remove and substituting the specific gene with the targeting vector by homologous recombination. Knockout pigs for various uses have been produced using these methods of constructing a targeting vector, and one can produce a knockout pig for various uses by constructing a targeting vector incorporating side portions of a sequence that are desired to be removed as flanking regions. That is, the vector of Day interposes a selection marker gene of G418 tolerance between exons 7 to 9 of a pig GT gene to knockout the GT gene. Therefore, using the vector of Day, live offspring from which exons 7 to 9 are removed are obtained.

In contrast to the methods of Day, the gene targeting vector construct of the subject invention contains a nucleic acid sequence corresponding to a part of intron 8, exon 9 and a part of intron 9 of a GT gene, and a nucleic acid sequence encoding a puromycin-resistant gene, wherein the puromycin-resistant gene substitutes a nucleic acid sequence corresponding to an AvaI-DraIII fragment of the exon 9. In this targeting vector, the puromycin-resistant gene is inserted in exon 9 of the GT gene by homologous recombination of the homologous fragment, thereby disrupting the GT gene.

Thus, the gene targeting vectors of the subject invention and those of Day are different in

construction and result in substantially different effects, and the cloned embryos or the transgenic cloned pigs that are produced by the introduction of each of these vectors also have substantially different phenotypes. That is, the vectors of Day result in live offspring consisting of genes from which exons 7, 8 and 9 are removed, but in the instant invention, live offspring consisting of genes from which exon 9 is removed are produced. Thus, the live offspring of the two inventions have substantially different genotypes that result in different phenotypes.

The instant invention provides methods of enabling heterograft without hyperacute immune rejection by providing organs of a cloned pig from which a GT gene is removed. For example, Example 13 of the instant specification discloses the production of three cloned pigs from which a GT gene is removed born 114 days after the embryonic transplantation, and Example 14 of the instant specification shows that a GT gene was absent from each of the three cloned pigs. That is, the inventors of the instant application obtained a total of three cloned pigs by introducing a targeting vector having a structure different form that of cited invention 1, and confirmed that all of those cloned pigs lack a functional GT gene thereby efficiently producing cloned pigs without a hyperacute immune rejection. Therefore, the homologous element included in the targeting vector is not merely a result of simple selection, but becomes a major factor that determines whether the objective of producing cloned pigs without a hyperacute immune rejection is achieved.

Furthermore, because the GT gene is inserted into a genome randomly even if an organ-specific promoter is used, it might not be expressed selectively only in a desired organ. To solve this problem, an organ-specific transgenic pig is produced using a BAC (bacterial artificial chromosome) clone. The BAC clone includes a promoter or an enhancer part that can be neglected, allowing the vector to reflect the nature of the original promoter. Therefore, the subject invention obtains a GT gene clone of a desired size by screening a BAC genomic library pool, which is dramatically differently from that of Day, which is obtained from the entire genome of a pig. The subject invention therefore may be used to produce an organ specific transgenic pig, which is a significant advance over the disclosure of Day.

Therefore, there is no motivation or teaching in Day to re-form the constituent sequences of the targeting vector to arrive at the vector of the instant application nor to use such a re-formulated vector to produce transgenic cells and offspring of the present invention.

Mason discloses a retrovirus vector particle containing an oncoretrovirus gag matrix protein that is varied to contain a nuclear localization signal to transform a non-dividing cell like a nerve cell. As indicated by the Examiner, Mason discloses a transgenic vector containing puromycin-resistant gene linked to a SV40 poly(A) sequence. However, the instant invention is directed to the removal of a GT gene from a cell that proliferates actively, while Mason teaches the introduction of a specific gene into a non-dividing cell like a nerve cell. Therefore, one of skill in the art would not supplement the teachings of Day nor the vectors and methods of the instant invention with the vector constructs of Mason as they are directed to entirely different purposes.

Similarly, Day teaches the removal of a GT gene from a cell that proliferates actively, while Mason, as noted above, teaches the introduction of a specific gene into a non-dividing cell like a nerve cell and therefore, there is no motivation to combine the disclosure of Mason and Day.

The Examiner has also rejected Claim 10 under 35 U.S.C. § 103(a) as being obvious over **Day** in view of **Mason** and further in view of **Zhao** (U.S. Patent Publication No. 2003/0092070). Zhao is cited for the disclosure of the use of FuGENE6 for transfection, but the disclosure of Zhao does not overcome the lack of motivation and the shortcomings of the teaching of the combination of Mason and Day described above.

Therefore, Applicants submit that there is no suggestion or motivation in the Mason and Day references to make the combination described by the Examiner and respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

Based upon the foregoing, Applicants believe that all pending claims are in condition for allowance and such disposition is respectfully requested. In the event that a telephone conversation would further prosecution and/or expedite allowance, the Examiner is invited to contact the undersigned.

Respectfully submitted,
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